Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Journal of Infection 80 (2020) 639–645

Contents lists available at ScienceDirect

Journal of Infection

journal homepage: www.elsevier.com/locate/jinf

Coronavirus disease 2019 in elderly patients: Characteristics and prognostic factors based on 4-week follow-up

Lang Wang[a,b,c,1], Wenbo He[a,b,c,1], Xiaomei Yu[a,b,c], Dalong Hu[d], Mingwei Bao[a,b,c], Huafen Liu[a], Jiali Zhou[a], Hong Jiang[a,b,c,*]

[a] Department of Cardiology, Renmin Hospital of Wuhan University, 238 Jiefang Road, Wuchang, Wuhan 430060, People's Republic of China
[b] Cardiovascular Research Institute, Wuhan University, Wuhan, People's Republic of China
[c] Hubei Key Laboratory of Cardiology, Wuhan, People's Republic of China
[d] School of Biotechnology and Biomolecular Sciences, The University of New South Wales, NSW 2052, Australia

ARTICLE INFO

Article history:
Accepted 15 March 2020
Available online 30 March 2020

Keywords:
Coronavirus infections
SARS-CoV-2
Pneumonia
Prognosis

SUMMARY

Objective: To investigate the characteristics and prognostic factors in the elderly patients with COVID-19.
Methods: Consecutive cases over 60 years old with COVID-19 in Renmin Hospital of Wuhan University from Jan 1 to Feb 6, 2020 were included. The primary outcomes were death and survival till March 5. Data of demographics, clinical features, comorbidities, laboratory tests and complications were collected and compared for different outcomes. Cox regression was performed for prognostic factors.
Results: 339 patients with COVID-19 (aged 71±8 years,173 females (51%)) were enrolled, including 80 (23.6%) critical, 159 severe (46.9%) and 100 moderate (29.5%) cases. Common comorbidities were hypertension (40.8%), diabetes (16.0%) and cardiovascular disease (15.7%). Common symptoms included fever (92.0%), cough (53.0%), dyspnea (40.8%) and fatigue (39.9%). Lymphocytopenia was a common laboratory finding (63.2%). Common complications included bacterial infection (42.8%), liver enzyme abnormalities (28.7%) and acute respiratory distress syndrome (21.0%). Till Mar 5, 2020, 91 cases were discharged (26.8%), 183 cases stayed in hospital (54.0%) and 65 cases (19.2%) were dead. Shorter length of stay was found for the dead compared with the survivors (5 (3–8) vs. 28 (26–29), $P < 0.001$). Symptoms of dyspnea (HR 2.35, $P = 0.001$), comorbidities including cardiovascular disease (HR 1.86, $P = 0.031$) and chronic obstructive pulmonary disease (HR 2.24, $P = 0.023$), and acute respiratory distress syndrome (HR 29.33, $P < 0.001$) were strong predictors of death. And a high level of lymphocytes was predictive of better outcome (HR 0.10, $P < 0.001$).
Conclusions: High proportion of severe to critical cases and high fatality rate were observed in the elderly COVID-19 patients. Rapid disease progress was noted in the dead with a median survival time of 5 days after admission. Dyspnea, lymphocytopenia, comorbidities including cardiovascular disease and chronic obstructive pulmonary disease, and acute respiratory distress syndrome were predictive of poor outcome. Close monitoring and timely treatment should be performed for the elderly patients at high risk.

Introduction

Corona Virus Disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections occurred in Wuhan in December 2019.[1] Till March 5, 2020, the SARS-CoV-2 infected 80,565 patients and caused 3015 deaths in China. Based on early statistical data of china, the case-fatality rate (CRF) in the patients over 60 years old is much higher than overall CRF, 14.8% CRF in patients over 80 years, 8.0% CRF in patients aged 70–79 years and 3.6% CRF in patients aged 60–69 years.[2] The proportion of deaths over 60 years old accounts for 81% of the total deaths in the national wide, which implicates aged people are more vulnerable to the SARS-CoV-2.

Till present there are rare reports in literature focusing on the clinical characteristics of the elderly patients with COVID-19, and the risk factors for poor outcomes remains to be elucidated. The present study aims to describe the clinical characteristics and to investigate the prognostic factors of the elderly patients with COVID-19, which might provide evidence for the risk stratification and help to improve the clinical practice and reduce fatality.

* Corresponding author at: Department of Cardiology, Renmin Hospital of Wuhan University, 238 Jiefang Road, Wuchang, Wuhan 430060, People's Republic of China.
E-mail address: hong-jiang@whu.edu.cn (H. Jiang).
[1] These two authors contributed equally to this work.

https://doi.org/10.1016/j.jinf.2020.03.019
0163-4453/

Patients and methods

Study design and participants

The study complied with the edicts of the Declaration of Helsinki and was approved by the Ethics Committee of Renmin Hospital of Wuhan University (No. WDRY2020-K032). Written informed consent was waived by the same committee. In this retrospective, single-center study, we included all confirmed cases of COVID-19 over 60 years old admitted from Jan 1 to Feb 6 at isolation ward of Renmin Hospital of Wuhan University in Wuhan, China. This is a designated hospital capable of receiving severe COVID-19 patients. All enrolled patients were diagnosed according to Interim guidance for novel coronavirus pneumonia published by National Health Commission of the People's Republic of China.[3] According to the report of the WHO–China Joint Mission on COVID-19,[4] patients with COVID-19 were divided into mild (laboratory confirmed, without pneumonia), moderate (laboratory confirmed and with pneumonia), severe (dyspnea, respiratory frequency $\geq$30/minute, blood oxygen saturation $\leq$93%, PaO2/FiO2 ratio $<$300, and/or lung infiltrates $>$50% of the lung field within 24–48 h) and critical (respiratory failure requiring mechanical ventilation, shock or other organ failure that requires intensive care).

Procedures

SARS-CoV-2 nucleic acid was detected in all patients by real-time PCR to confirm the virus infection. Chest X-ray and/or computed tomography were performed for the diagnosis of pneumonia. Patients' medical records were carefully reviewed and analyzed by three trained physicians. Patient data including demographics, comorbidities, signs and symptoms, laboratory results and complications were obtained. Patient history were collected for comorbidities including hypertension, diabetes, cardiovascular disease, cerebrovascular disease, chronic kidney disease, chronic liver disease, chronic obstructive pulmonary disease (COPD), malignancy and autoimmune diseases.

The occurrence of complications was confirmed by three physicians according to the following criteria. Acute kidney injury was identified according to the Kidney Disease: Improving Global Outcomes of Definition.[5] Cardiac injury was defined if the serum level of cardiac troponin I (cTnI) was above the 99th percentile upper reference limit. ARDS was defined according to the Berlin definition.[6] Arrhythmia was defined as emerging premature beat, tachycardia, atrial fibrillation, ventricular fibrillation and clinically significant bradycardia according to electrocardiography or medical records, transient sinus tachycardia associated with fever was excluded. Cardiac insufficiency was defined when the serum level of NT-pro BNP exceeded the normal range and the presence of associated symptoms, such as dyspnea, orthopnea and edema of lower extremity. The interval from symptom onset to admission and the length of stay were also recorded.

Outcomes

The primary outcomes were survival and death till March 5, 4 weeks from the last admission. Patients cured were discharged when the symptoms improved significantly, with no fever for at least three days, obvious absorption of inflammation in pulmonary imaging, and negative results for at least two consecutive tests of SARS-CoV-2 nucleic acid. Patients who didn't meet the discharge standard continued hospitalization for treatment and observation. The patients discharged or stayed in hospital till the end date of follow-up were classified into survival group.

Statistical analysis

Basic statistical analyses were performed using SPSS version 17.0. The normality of continuous variables was tested using the Kolmogorov-Smirnov test. Hypothesis testing was performed for comparing continuous and categorical variables in different outcome groups using Mann-Whitney U test and Chi-squared test respectively. The clinical and laboratory variables, which differed significantly under comparative statistics, were included in a univariate Cox analysis (proportional hazards regression) using R language v3.5.2 with packages "survival" and "survminer". The models used in the univariate analysis were tested by Likelihood ratio test, Wald test and Score (log-rank) test. Multivariate Cox regressions were subsequently performed for comorbidities and complications, in which the "Age" factor was added to correct the models and only variables with statistical significance in univariate analysis were included. All significance levels were computed for 2-tailed testing and the cutoff of significance was set at $P < 0.05$.

Results

Demographics and baseline clinical characteristics

Of 339 patients identified, the mean age was 71 years, and 173 were female (51%). As presented in Table 1, 60.7% of the patients had comorbidities, while 23.9% had two or more comorbidities. Common comorbidities included hypertension (138 cases, 40.8%), diabetes (54 cases, 16.0%) and cardiovascular disease (48 cases, 14.2%). The most common symptom was fever, which occurred in 311 (92%) patients. Symptoms such as cough (179 cases, 53.0%), dyspnea (138 cases, 40.8%) and fatigue (135 cases, 39.9%) were also prevalent in those patients. Till Mar 5, 2020, 91 cases were discharged (26.8%), 183 cases (54.0%) stayed in hospital and 65 cases (19.2%) were dead. The median duration of hospital stays for the discharged was 21 days (interquartile range, 15–26). The patients discharged or stayed in hospital till the end date of follow-up were classified into survival group. Compared with the survival subjects, there were fewer women in the dead group and the dead patients were significantly older. Comorbidities including hypertension, cardiovascular disease, cerebrovascular disease, and COPD were more prevalent in the dead group. It should be noted that there were more patients complaining of dyspnea in the dead group (38/65 vs. 100/274, $p < 0.001$). In addition, fever and headache were less common in patients who died. Considering the vital signs, significant higher respiration rates were found in the dead group, in comparison to the survived.

Laboratory findings

Of the included 339 patients, lymphocytopenia was found in 211 cases (63.2%). The counts of $CD4^+$ and $CD8^+$ cells were all decreased compared with normal values. The comparisons of laboratory findings between the survival and dead group were shown in Table 2. When compared with the survival group, the count of neutrophils was significantly increased, while the counts of lymphocyte, monocyte and platelet were decreased. The counts of $CD4^+$ and $CD8^+$ *T* cells, which play important role in antiviral immunity,[7,8] were all significantly decreased in the dead group. The prothrombin time was significantly prolonged, and the concentration of D-dimer was evidently increased in the dead group. The alanine aminotransferase, an important indice for liver function, showed no evident difference between survival and death. At the same time, serum urea and creatinine levels were observed to be higher in the dead group. In addition, the markers for myocardial injury, inflammation, and bacterial infections were all increased significantly in the dead group.

Table 1
Demographic data and baseline clinical characteristics.

Characteristics	Total ($n = 339$)	Survival ($n = 274$)	Dead ($n = 65$)	P value (Dead vs. Survival)
Age, median (IQR), y	69 (65–76)	68 (64–74)	76 (70–83)	<0.001
Female gender	173 (51.0)	147 (53.6)	26 (40.0)	0.048
Comorbidities				
Hypertension	138 (40.8)	106 (38.8)	32 (50.0)	0.031
Diabetes	54 (16.0)	43 (15.8)	11 (17.2)	0.116
Cardiovascular disease	53 (15.7)	32 (11.7)	21 (32.8)	<0.001
Cerebrovascular disease	21 (6.2)	11 (4.0)	10 (15.6)	<0.001
Chronic kidney disease	13 (3.8)	9 (3.3)	4 (6.3)	0.066
Chronic liver disease	2 (0.6)	1 (0.4)	1 (1.6)	0.065
COPD	21 (6.2)	10 (3.7)	11 (17.2)	<0.001
Malignancy	15 (4.4)	12 (4.4)	3 (4.7)	0.12
Autoimmune disease	5 (1.5)	4 (1.5)	1 (1.6)	0.121
Symptoms				
Fever	311 (92.0)	255 (93.4)	56 (87.5)	0.041
Dry cough	179 (53.0)	149 (54.6)	30 (46.9)	0.068
Expectoration	93 (27.5)	76 (27.8)	17 (26.6)	0.119
Fatigue	135 (39.9)	109 (39.9)	26 (40.6)	0.12
Anorexia	94 (27.8)	79 (28.9)	15 (23.4)	0.083
Myalgia	16 (4.7)	15 (5.5)	1 (1.6)	0.05
Dyspnea	138 (40.8)	100 (36.6)	38 (59.4)	<0.001
Pharyngalgia	13 (3.9)	10 (3.7)	3 (4.7)	0.112
Diarrhea	43 (12.7)	35 (12.8)	8 12.5)	0.121
Nausea	13 (3.8)	12 (4.4)	1 (1.6)	0.07
Chest tightness	88 (26.0)	73 (26.7)	15 (23.4)	0.105
Dizziness	13 (3.8)	11 (4.0)	2 (3.1)	0.114
Headache	12 (3.5)	12 (4.4)	0 (0.0)	0.029
Vital signs				
Heart rate, median (IQR), (bpm)	82 (77–91)	82 (76–90)	84 (78–101)	0.063
SBP, median (IQR), (mmHg)	130 (119–142)	130 (120–140)	130 (114–152)	0.519
DBP, median (IQR), (mmHg)	76 (70–83)	76 (70–82)	76 (65–90)	0.938
Respiration rate, median (IQR), (times per min)	20 (18–21)	20 (18–20)	21 (18–30)	<0.001

Continuous variables were expressed as median (interquartile range) and categorical variables were expressed as number (percentage). COPD, chronic obstructive pulmonary disease; DBP, diastolic blood pressure; IQR, interquartile range; SBP, systolic blood pressure.

Table 2
Laboratory findings of patients with different outcomes.

Laboratory tests	Normal Range	Total ($N = 339$)	Survival ($n = 274$)	Dead ($n = 65$)	P value (Dead vs. Survival)
Blood Routine					
White blood cell count, $\times 10^9$/L	3.5–9.5	5.74 (4.37–8.29)	5.54 (4.29–7.64)	8.61 (5.27–13.25)	<0.001
Neutrophil count, $\times 10^9$/L	1.8–6.3	4.43 (2.76–6.62)	4.01 (2.63–5.97)	7.65 (4.35–11.74)	<0.001
Lymphocyte count, $\times 10^9$/L	1.1–3.2	0.90 (0.59–1.29)	0.97 (0.68–1.37)	0.57 (0.39–0.84)	<0.001
Monocyte count, $\times 10^9$/L	0.1–0.6	0.42 (0.28–0.59)	0.43 (0.30–0.62)	0.32 (0.22–0.49)	0.007
Hemoglobin concentration, g/L	130–175	121 (109–130)	121 (110–129)	122 (106–137)	0.434
Platelet count, $\times 10^9$/L	125–350	205 (151–259)	211 (159–268)	172 (103–219)	<0.001
Blood Coagulation					
Prothrombin time, s	9–13	12.1 (11.6–12.7)	12.0 (11.6–12.6)	12.9 (11.9–14.1)	<0.001
Activated partial thromboplastin time, s	25–31.3	28.5 (26.2–31.3)	28.3 (25.6–31.2)	29.1 (27.4–31.8)	0.072
D-dimer, mg/L	0–0.55	1.20 (0.62–3.25)	1.08 (0.52–2.05)	4.38 (1.32–17.01)	<0.001
Blood Biochemistry					
Alanine aminotransferase, U/L	9–50	27 (17–44)	28 (17–43)	24 (19–49)	0.83
Aspartate aminotransferase, U/L	15–40	32 (23–46)	29 (22–43)	43 (30–68)	<0.001
Urea, mmol/L	3.6–9.5	5.5 (4.0–8.0)	5.1 (3.9–7.0)	8.9 (6.0–14.2)	<0.001
Creatinine, μmol/L	57–111	61 (50–76)	60 (49–71)	80 (55–114)	<0.001
Creatine kinase, U/L	50–300	63 (40–104)	60 (40–97)	84 (50–222)	0.005
Lactate dehydrogenase, U/L	120–250	301 (224–429)	286 (220–355)	439 (360–643)	<0.001
Myocardial Injury Markers					
Creatine kinase-MB, ng/mL	0–5	1.26 (0.85–2.36)	1.15 (0.81–1.91)	2.95 (1.30–4.30)	<0.001
Hypersensitive troponin I, ng/mL	0–0.04	0.010 (0.006–0.030)	0.007 (0.006–0.018)	0.073 (0.023–0.336)	<0.001
Inflammatory Markers					
C-reactive protein, mg/L	0–10	49.6 (18.5–93.2)	44.2 (13.5–82.2)	102.0 (58.9–187.4)	<0.001
Interleukin-6, pg/mL	<10	10.9 (5.2–25.4)	10.5 (4.9–18.8)	93.8 (35.9–182.3)	<0.001
Cellular immunity					
CD4+ cell count, /μl	404–1612	314 (190–484)	349 (217–516)	191 (107–282)	<0.001
CD8+ cell count, /μl	220–1129	179 (85–286)	204 (97–298)	73 (42–160)	<0.001
Bacterial Infection Marker					
Procalcitonin, ng/mL	<0.1	0.08 (0.04–0.17)	0.06 (0.04–0.13)	0.22 (0.11–1.13)	<0.001

The variables were expressed as median (interquartile range) and compared using Mann-Whitney U test.

Table 3
Spectrum of disease and complications.

	Total ($n=339$)	Survival ($n=274$)	Dead ($n=65$)	P value (Dead vs. Survival)
Spectrum of Disease				
Moderate	100 (29.5)	99 (36.1)	1 (1.5)	<0.001
Severe	159 (46.9)	155 (56.6)	4 (6.2)	
Critical	80 (23.6)	20 (7.3)	60 (92.3)	
Complications				
Bacterial Infection	143 (42.8)	94 (34.4)	49 (81.7)	<0.001
AKI	27 (8.1)	11 (4.0)	17 (28.3)	<0.001
ARDS	71 (21.0)	15 (5.5)	56 (87.5)	<0.001
Liver Enzyme Abnormalities	96 (28.7)	74 27.1)	22 (36.7)	<0.001
Acute cardiac injury	70 (21.0)	31 (11.4)	39 (65.0)	<0.001
Arrhythmia	35 (10.4)	22 (8.1)	13 (20.6)	<0.001
Cardiac insufficiency	58 (17.4)	33 (12.1)	25 (42.4)	<0.001
Shock	8 (2.4)	5 (1.8)	3 (4.7)	0.049

The variables were expressed as number (percentage) and compared with Chi-squared test. AKI, acute kidney injury; ARDS, acute respiratory distress syndrome.

Table 4
Duration of disease onset to admission and hospital stays.

	Total ($N=339$)	Survival ($N=274$)	Dead ($N=65$)	P value (Dead vs. Survival)
Symptom onset to admission, median (IQR), days	10 (7–14)	10 (7–13)	10 (7–14)	0.532
Hospital stay, median (IQR), days	28 (15–28)	28 (26–29)	5 (3–8)	<0.001

The variables were expressed as median (IQR) and compared using Mann-Whitney U test. IQR, interquartile range.

Spectrum of disease and complications

Renmin Hospital of Wuhan University is a designated hospital for severe COVID-2019 patients. As described in Table 3, in the present study, 70.5% of the enrolled patients are classified as severe or critical. Almost all of the dead patients were critically ill (92.3%), only four severe patients died till the end of follow-up. Only one death was found in moderate cases, which was due to sudden cardiac death.

During hospital stay, bacterial infection was found in 143 cases (42.8%), liver enzyme abnormalities were observed in 96 cases (28.7%), and acute respiratory distress syndrome (ARDS) occurred in 71 (21.0%) patients. 70 patients had acute cardiac injuries (21.0%). The incidences of all the complications were significantly higher in the dead group in comparison to the survivors.

The duration of onset-to-admission and hospital stays

The interval time from symptom onset to admission was recorded for each patient (Table 4). There was no significant difference between the survival and dead group. Given that the final length of hospital stays for the patients remained in hospital was unknown, the duration for those patients was calculated from admission to the end date of follow-up. The results showed that the length of hospital stay was dramatically shorter for the dead patients. The median duration of hospitalization was only 5 days in the dead group, which was significantly shorter than that in the survival group (5 (3–8) vs. 28 (26–29), $P < 0.001$).

Prognostic factors of the elderly COVID-19 patients

Univariate Cox regression was used to analyze the risk factors for fatal outcomes in the elderly patients with COVID-19 (Fig. 1), the hazard ratio (HR) and 95% confidence interval (CI) were shown in the columns right to the chart. Older age was shown to increase the likelihood of death even in elderly patients (HR 1.08, CI 1.06–1.11, $P < 0.001$). Symptoms of dyspnea (HR 2.35, CI 1.43–3.87, $P=0.001$) and comorbidities including cardiovascular disease (HR 2.87, CI 1.70–4.83, $P < 0.001$), cerebrovascular disease (HR 3.26, CI 1.66–6.40, $P=0.001$) and COPD (HR 3.72, CI 1.94–7.13, $P < 0.001$) were all predictive of fatal outcomes. Complications including acute cardiac injury, arrhythmia, acute kidney injury (AKI), ARDS, cardiac insufficiency and bacterial infection were all predictors of death. The models used in the univariate analysis were tested by Likelihood ratio test, Wald test and Score (log-rank) test and all the three methods supported the significance of the models. Then the "Age" factor was added to correct the models for the multi-factor regressions of comorbidities and complications (Fig. 2). In the multi-factor analysis, only cardiovascular disease (HR 1.86, CI 1.06–3.26, $P=0.031$), COPD (HR 2.24, CI 1.12–4.50, $P=0.023$) and ARDS (HR 29.33, CI 12.37–69.58, $P < 0.001$) remained to be the predictors for death when other factors in the model kept constant, while the contributions of other factors were no longer significant in the model. Among the vital signs, increased heart rate and respiration rate could increase the likelihood of fatal outcomes. For the laboratory tests, white blood cell count (HR 1.16, CI 1.14–1.20, $P < 0.001$) and prothrombin time (HR 1.17, CI 1.13–1.24, $P < 0.001$) were shown to increase the risk of death, and a low level of lymphocytes was a strong predictor of poor outcome (HR 0.10, CI 0.04–0.22, $P < 0.001$). Significances were also found in other factors such as procalcitonin and hypersensitive troponin I. However, for those factors the HR was around 1.0, which limited their values as predictors.

Discussion

In the present study, we described the clinical characteristics of elderly COVID-19 patients who were faced with the highest risk of death after SARS-CoV-2 infection. And we investigated the prognostic factors of COVID-19 based on at least 4 weeks of follow-up. SARS-CoV-2 caused a much more severe pneumonia in the aged people than younger patients. Of the 339 elderly COVID-19 patients included, over 70% were severe or critical, and the case fatality rate was 19%. Fast progress of disease was found in the dead with a median survival time of 5 days after admission. Several factors were found to be predictors for poor outcomes, such as symptom of dyspnea, comorbidities like cardiovascular disease and COPD, and complications like ARDS. It should be noted that once ARDS occurred, the probability of death would increase dramatically. On the other side, increased lymphocyte count was predictive of better outcomes.

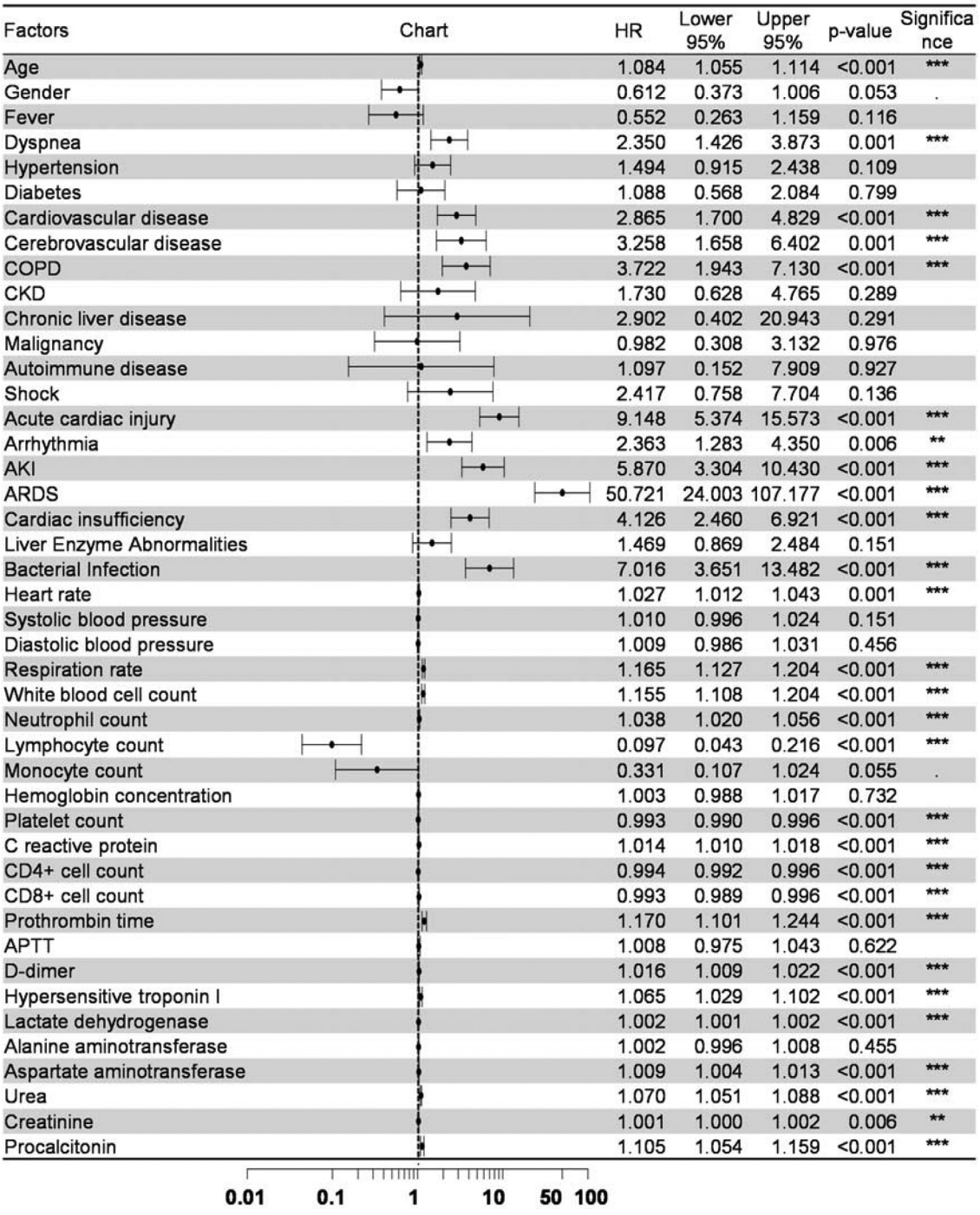

Fig. 1. Univariate Cox regression for prognostic factors.
Univariate Cox regression analysis of risk factors associated with fatality. AKI, acute kidney injury; APTT, activated partial thromboplastin time; ARDS, acute respiratory distress syndrome; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; HR, hazard ratio. $^{**}P < 0.01$, $^{***}P < 0.001$.

The distinct features of COVID-19 in these included elderly patients were evidently increased severity and fatality. The reported proportion of severe-to-critical patients in the whole population was 18.5% and the case-fatality rate was 2.3%,[9] significantly lower than the present study. As Renmin Hospital of Wuhan University was a designated hospital for severe COVID-19 patients, the proportion of severe and critical patients and fatality rate might be different from other centers. In the 65 dead cases 92.3% were critically ill. The only one death in moderate cases was caused by sudden cardiac death. As indicated by the short length of stay (median, 5 days) for the dead, the disease progressed considerably fast for those patients. The most common symptoms at admission were fever, cough, dyspnea and fatigue, which was consistent with the general symptoms of viral infection and pneumonia. Dyspnea was more prevalent in the dead patients. In consistence, the respiration rate at admission was significantly higher in the dead group compared with survival group. The incidence of comorbidities was relatively higher in the elderly COVID-19 patients compared with the whole population.[9] The most common comorbidities were hypertension, diabetes, cardiovascular disease and cerebrovascular disease. The median heart rate, blood pressure and respiration rate were in the normal range at admission both in survival and dead

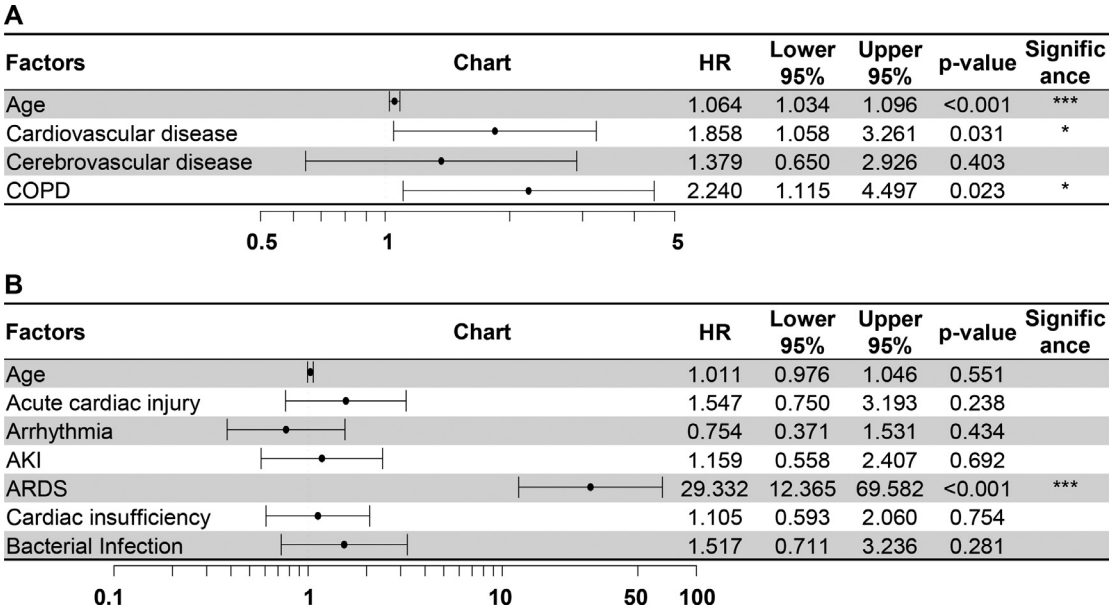

Fig. 2. Multivariate Cox regression for prognostic factors.
Multivariate Cox regressions were performed for comorbidities (A) and complications (B), in which the "Age" factor was added to correct the models. AKI, acute kidney injury; ARDS, acute respiratory distress syndrome; COPD, chronic obstructive pulmonary disease; HR, hazard ratio. $^{*}P < 0.05$, $^{***}P < 0.001$.

group, indicating that the vital signs of most patients were stable at admission. Common complications during hospitalization were bacterial infection, liver enzyme abnormalities, ARDS and acute cardiac injury.

Significant differences were found in laboratory findings between the dead and survivors. Generally, evident decrease of lymphocytes was observed in the dead group. Specifically, the count of $CD4^{+}$ and $CD8^{+}$ lymphocytes were both significantly reduced in the dead group, indicating the suppressed cellular immunity in these patients. At the same time, more severe inflammatory reactions might exist in the dead cases as represented by significant increase of inflammatory markers. In addition, more frequent coagulation disorders, myocardial injuries and bacterial infections were found in the dead group compared to the survival group, as revealed by the related markers. Compared with the survivors, serum concentrations of urea and creatinine were higher in the dead, indicating worse renal functions, although the median values were still within the normal range.

As found by the cox regression, there were several prognostic factors in the elderly COVID-19 patients. Dyspnea and high respiration rates were probably manifestations for impaired respiratory function and might reflect the severity of lung lesions caused by infection or inflammation. The impaired oxygenation caused by COVID-19 brings great challenge to the cardiopulmonary function, especially for the elderly. Comorbidities such as cardiovascular disease and COPD could greatly increase the vulnerability of elderly patients when faced with this disease. It is reasonable that these factors could predict poor outcomes. ARDS, the fundamental pathophysiology of severe viral pneumonia, could be a marker of rapid progress of the disease. Once ARDS occurred, the 28-day mortality would be near 50%.[10] Consistent with that, in the present study, the occurrence of ARDS was an extremely strong predictor of fatal outcomes, which could increase the probability of death by a factor of 29.3. In laboratory tests, lymphocytopenia were found in around 60% of the overall patients and in 81.5% of the dead patients, which was similar with previous studies on SARS.[11] It has been reported that lymphocytes could be killed by coronavirus due to the damage of the cytoplasmic components or apoptosis.[12,13] The degree of lymphocytopenia might reveal either the severity of virus invasion or the condition of the antiviral immunity, thus could predict the outcome.

According to the above, patients' conditions on admission including dyspnea, comorbidities of cardiovascular disease and COPD, lymphocytopenia, and ARDS during hospitalization, could predict the risk of death. These factors should be considered for risk stratification. We have found that COVID-19 progressed rapidly for some severe or critical patients. Therefore, for the elderly patients the risk factors should be taken into consideration. For those at high risk, close monitoring and timely treatment might be very important and could help to improve the outcome.

Limitations

This study has several limitations. As Renmin Hospital of Wuhan University was a designated hospital for severe COVID-19 patients, the proportion of severe and critical patients and fatality rate might be different from the whole infected population. In addition, as a retrospective study on a severe disease, some relevant data such as interleukin-6 were incomplete and could not be included in the risk factor analysis.

Conclusions

High proportion of severe to critical cases and high fatality rate were observed in the elderly patients with COVID-19. Rapid progress of disease was noted in the dead patients with a median survival time of 5 days after admission. Patients' conditions on admission such as dyspnea, lymphocytopenia, cardiovascular disease and COPD, and the occurrence of ARDS during hospitalization were predictive of fatal outcome. Close monitoring and timely treatment should be performed for the elderly patients at high risk.

Declaration of Competing Interest

The authors declare that there is no conflict of interests.

Acknowledgements

This work was supported by the National Natural Science Foundation of China Grant numbers 81570450, 81900455.

References

1. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;**395**(10223):497–506.
2. Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020.
3. . *Interim guidance for novel coronavirus pneumonia*. 6th Ed. National Health Commision of the People's Republic of China; 2020 *http://www.nhc.gov.cn/yzygj/s7653p/202002/8334a8326dd94d329df351d7da8aefc2.shtml* Accessed February 27th, 2020.
4. Report of the WHO-China Joint Mission on Coronavirus Disease; 2019 *https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report* Accessed Mar 5th, 2020.
5. Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. *Nephron Clin Pract* 2012;**120**(4):c179–84.
6. Ferguson ND, Fan E, Camporota L, et al. The berlin definition of ARDS: an expanded rationale, justification, and supplementary material. *Intensive Care Med* 2012;**38**(10):1573–82.
7. Jansen JM, Gerlach T, Elbahesh H, Rimmelzwaan GF, Saletti G. Influenza virus-specific CD4+ and CD8+ T cell-mediated immunity induced by infection and vaccination. *J Clin Virol* 2019;**119**:44–52.
8. Whitmire JK, Ahmed R. Costimulation in antiviral immunity: differential requirements for CD4(+) and CD8(+) t cell responses. *Curr==70==. Opin Immunol* 2000;**12**(4):448–55.
9. . The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China. *Zhonghua Liu Xing Bing Xue Za Zhi* 2020;**41**(2):145–51.
10. Bellani G, Laffey JG, Pham T, et al. Epidemiology, patterns of care, and mortality for patients with acute respiratory distress syndrome in intensive care units in 50 countries. *JAMA* 2016;**315**(8):788–800.
11. Zumla A, Hui DS, Perlman S. Middle east respiratory syndrome. *Lancet* 2015;**386**(9997):995–1007.
12. Gu J, Gong E, Zhang B, et al. Multiple organ infection and the pathogenesis of Sars. *J Exp Med* 2005;**202**(3):415–24.
13. Chu H, Zhou J, Wong BH, et al. Middle east respiratory syndrome coronavirus efficiently infects human primary t lymphocytes and activates the extrinsic and intrinsic apoptosis pathways. *J Infect Dis* 2016;**213**(6):904–14.